Cost Savings Resulting from NIH Research Support

A periodic evaluation of the cost-benefits of biomedical research

U.S. DEPARTMENT OF HEALTH AND HUMAN SERVICES
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CC Warren Grant Magnuson Clinical Center

NCI National Cancer Institute

NEI National Eye Institute

NHLBI National Heart, Lung, and Blood Institute

NIAID National Institute of Allergy and Infectious Diseases

NIAMS National Institute of Arthritis and Musculoskeletal and Skin Diseases

NICHD National Institute of Child Health and Human Development

NIDDK National Institute of Diabetes and Digestive and Kidney Diseases

NINDS National Institute of Neurological Disorders and Stroke

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The Office of Science Policy and Legislation's Research Results Assessment Program (RRAP) has examined instances of health care advances resulting from NIH support for applied research and clinical trials as a part of its periodic evaluation of the cost-benefits of biomedical research. In collaboration with the Institutes, Centers, and Divisions, 26 examples have been identified to date. These advances have had considerable impact on improvement in quality of life and reduction in morbidity and premature mortality, which in turn have been translated into significant cost savings.

Basic research is not included in this assessment. It is clear, however, that the scientific advances would not have been possible without the continuing insights and understandings regarding the fundamental mechanisms of life and disease made possible by NIH-supported basic research. It is equally clear that basic research linkages to health care advances are complicated, long-term, and impossible to allocate clearly.

A short technical appendix that outlines the cost calculation methodology can be found at page 24 for those interested in the more technical details of such calculations.

Examples

Close to 900 newborns can be saved annually from a lifetime of arrested physical and mental development through the development of a mass screening device for neonatal hypothyroidism. The total NIH costs for targeted applied research and clinical trials have been estimated at about $1.2 million with a potential 1-year savings of over **$206 million**.

The development of laser photocoagulation treatment of diabetic retinopathy has been shown through clinical trials to be effective in reducing the risk of severe visual loss from advanced stages of diabetic retinopathy, as well as from diabetic macular edema, another retinal complication of diabetes. The potential 1-year net present value savings is over **$2 billon**. The total NIH investment for a clinical trial was $48.2 million.

During the last decade, NIH-supported research has identified the metabolic abnormalities which underlie the formation of kidney stones. This in turn has led to the development of a relatively simple and inexpensive potassium citrate treatment for preventing recurrence of kidney stones among the estimated 198,000 patients susceptible to such a condition. Slightly over $679,000 was expended for research grants to pay for the research effort. It is estimated that close to **$300 million** in annual treatment costs and lost work days can be saved from this advance.

Validation of the advantages of outpatient breast biopsies has made possible a two-stage breast cancer procedure that provides an alternative for more than 490,000 women annually who would otherwise suffer the anguish and uncertainty of combined diagnosis and treatment under general anesthesia. A total of $10.6 million of the NCI National Surgical Adjuvant Breast Project was expended from 1971 to 1986 to perfect this procedure. Potential 1-year reduced diagnosis and treatment costs are estimated at upwards of **$169 million**.

Demonstration that medical management for patients with stable class I or II angina not suffering from either congestive heart failure or reduced left ventricular function entails no risk so that bypass surgery can be safely postponed until the onset of worsening symptoms. The total costs of the Coronary Artery Surgery Study (CASS) between 1973 and 1984 amounted to $27 million. Depending on the rate of adoption and the proportion of the bypass cases postponed, the savings can range from **$258 million** to **$516 million**.

Testicular cancer is the most common malignancy in 15-to 35-year-old males and is the most frequent cause of cancer-related deaths in this age group. The development of cisplatin in combination therapy has provided new hope for victims of this disease. The treatment significantly increases the survival rate and reduces workdays lost due to premature mortality and morbidity. This translates into a potential 1-year savings for the nation of upwards of **$109 million**. NIH funds invested over a 17-year period in the discovery and development of cisplatin for treatment of testicular cancer amounted to less than $56 million.

An improved vaccine for the prevention of haemophilus influenza type b (Hib) disease in the 18-month to 5-year age group has been developed with NIH funds. Hib is a leading cause of bacterial meningitis in the United States. Prevention of meningitis also protects a number of surviving children from a variety of neurological sequelae, including hearing loss, vision impairment, mental retardation and seizure disorders. The estimated net cost savings realizable from the reduction in premature mortality and elimination of long-tern earning losses are over **$109 million** annually. Total NIH research support during a 17-year period was $15.6 million.


AIDS Protocol
Precautions

NIH funds helped to develop an assay for detection of HIV antibodies in the sera of individuals exposed to the HIV virus. Screening of blood donors is estimated to save 891 transfusion recipients from HIV infection annually. This translates into a potential 1-year savings of over **$47 million**. The total NIH expenditure for the development and evaluation of the blood test from 1984-1989 was $6.7 million.

Adjuvant therapy with levamisole and 5-fluorouracil (5-FU) was developed for Dukes' C colon cancer. This new treatment significantly delays tumor recurrence and reduces patient risk of dying of recurrent colon cancer by one-third. Over 22,000 patients are diagnosed with this condition annually. Potential cost savings resulting from reduction of premature mortality and lost work days add up to close to **$136 million** annually. Total NIH investment since 1978 has amounted to $10.8 million.

Development of a combined cytotoxic drug and steroid treatment for patients suffering nephritis resulting from systemic lupus erythematosus has been found to sustain life-supporting renal function beyond 5 years at a considerably greater rate than earlier interventions. This provides hope for the more than 1,000 nephritis victims who each year are afflicted with this disorder. The realizable annual cost savings associated with this advance are estimated at close to **$70 million**. The NIH support has totaled $9.8 million since 1970.

The remaining examples involve other advances in diagnosis, improved therapy, development of vaccines or effective chemotherapeutic agents, and confirmation of ineffectual or inappropriate current practice. Realizable annual cost savings for these examples range from a low of **$2.6 million** to **$341 million**. All 26 examples are listed in the following pages.

Health Care Cost Savings Resulting from NIH-Supported Research 1986

Health Care Advance

NHLBI compared advantages of medical vs. surgical treatment. The Coronary Artery Surgery Study results indicated that bypass surgery could be deferred in some patients in favor of established medical management approaches. Estimates of savings are based on statistics from the trial in 1983. The current rate of adoption is not known.

NHLBI developed antenatal steroid therapy to prevent neonatal respiratory distress syndrome. Estimates of the savings have a wide variance due to uncertainty about neonatal length-of-stay in intensive care and the current rate of adoption is not known.

NHLBI improved preparation of blood for transfusing Cooley's anemia patients. The innovation will benefit all patients with transfusion dependent anemias, patients on cancer chemotherapy, and patients with chronic renal failure.

CC developed orthosis for joint dysfunction. The innovation provided a nonsurgical option to approximately 5,000 persons annually. The rate of adoption may now have exceeded 50 percent.

CC is now able to salvage previously unusable blood. The American Association of Blood Banks has proposed revising its standards to allow adoption of this innovation.

NIAID formulated the hepatitis B vaccine. The vaccine was licensed in 1982. Cost savings approximations are based on estimated incidence in 1983. The target population for immunization is the high-risk group in which 50 percent of the illness occurs yearly. The current rate of adoption is not yet known.

Estimated Amount and Duration of NIH Applied and Clinical Research Support (millions $)	Estimated Potential 1 Year Savings (millions $ and type of savings)
$27 (1973 - 1984)	$258 - $516 Reduces cost of treatment
$5.5 (1976 - 1983)	$10.6 - $93.1 Reduces cost of treatment
$0.39 (1983 - 1986)	$1.8 - $2.6 Reduces cost of treatment
$0.37 (1984 - 1986)	$13.4 - $26.7 Reduces cost of treatment
$0.016 (1983 - 1984)	$1 - $2 Reduces cost of treatment
$23.5 (1964 - 1981)	$47.3 - $94.7 Prevents acute, chronic illness/ reduces health care utilization

NIAID developed the varicella vaccine to prevent chickenpox in immunocompromised children. The clinical trial is currently continuing; the vaccine is not yet licensed in the U.S. Estimates of maximum potential cost savings assume that the vaccine will be fully utilized in juvenile patients with leukemia and lymphomas (1,500 per year).

NINDS confirmed the efficacy of the overall plasmapheresis treatment procedure (removal of selected materials from the bloodstream) to expedite recovery from the Guillain-Barré syndrome. About 2,000 patients per year are candidates for such treatment. Depending on the adoption rate for the procedure, annual savings range from **$18.1** to **36.2 million**.

NINDS determined that there was little clinical value to extracranial-intracranial arterial bypass surgery for ischemic cerebral vascular disease. There were approximately 2,000 such procedures performed in 1985 when the study results were announced. It was estimated that a 50 percent reduction in the surgery might occur in 1986, with a possible annual savings of **$13.8 million**.

NCI developed a two-stage diagnosis-treatment of breast cancer. Evidence indicates that one-half of patients with diagnosed breast cancer have the two-stage procedure. The savings from this innovation arise from the patients with benign lesion who have only the first stage (outpatient biopsy).

NEI evaluated laser photocoagulation treatment of diabetic retinopathy through clinical trials. Although one of the trials is continuing today, the example assumes 100 percent adoption of this innovation.

Estimated Amount and Duration of NIH Applied and Clinical Research Support (millions $)	Estimated Potential 1 Year Savings (millions $ and type of savings)
$1.8 (1979 - 1986)	$5.4 Reduces cost of treatment
$3.3 (1981 - 1984)	$18.1 - $36.2 Reduces cost of treatment
$9 (1977 - 1985)	$13.8 Reduces cost of treatment
$10.6 (1971 - 1986)	$168.9 - $337.9 Reduces cost of treatment
$48.2 (1971 - 1986)	$2,300.0 [1/] Reduces risk of vision loss

NICHD utilized mass screening for neonatal hypothyroidism. Due to the mass screening, 97 percent of infants with congenital hypothyroidism are identified in time to prevent mental retardation.

NIDDK discovered preventive measures for the recurrence of kidney stones. The drug (potassium citrate) was approved by the FDA in 1985 and is now being marketed. The current rate of adoption is not known.

Estimated Amount and Duration of NIH Applied and Clinical Research Support (millions $)	Estimated Potential 1 Year Savings (millions $ and type of savings)
$1.2 (1979 - 1986)	$206.2 [2/] Prevents chronic disease
$0.68 (1980 - 1984)	$299.8 - $599.7 Reduces cost of treatment

[1/] *Present value of cumulative $2,800 million savings over 5 years, discounted at 6 percent.*

[2/] *Present value of cumulative $625 million cost savings over first 65 years of age of first-year cohort, discounted at 6 percent.*

Health Care Cost Savings Resulting from NIH-Supported Research 1988

Health Care Advance

NIAID improved the treatment regimen for bee sting allergy. The research demonstrated that conventional life-long therapy for bee sting allergy was no better than a placebo. It was also proved that therapy based on bee venom was effective and required only 5 years of treatment. Major savings are from the elimination of inappropriate treatment for 250,000 persons per year.

NICHD decreased tonsillectomies. The Pittsburgh Tonsillectomy and Adenoidectomy Study was designed to overcome flaws in previous controlled studies. It demonstrated that the operation was not indicated in the great majority of cases. Example conservatively attributes 50 percent of the reduction from 1981 to 1987 in the rate of tonsillectomies performed in hospitals to the NIH supported study.

NHLBI conducted a study demonstrating that high-dose methylprednisolone (MPSS) neither prevents adult respiratory distress syndrome (ARDS) nor reduces mortality, and that treatment may cause adverse side effects. Savings are due to the expected elimination of ineffective treatment for an estimated 75,000 patients per year with septic shock.

NINDS conducted febrile seizure studies. Medical opinion has been sharply divided concerning the management of febrile seizures. The net result of the NIH sponsored work was that less than 10 percent of all children who experience one febrile seizure need to be treated with chronic anticonvulsant therapy. Savings are due to an expected reduction in the intensity of treatment.

Estimated Amount and Duration NIH Applied and Clinical Research Support (millions $)	Estimated Potential * 1 Year Savings (millions $ and type of savings)
$8.33 (1969 - 1989)	$52.8 - 70.4 Reduces cost of ineffectual treatment
$8.03 (1973 - 1987)	$208.8 - $278.4 Reduces cost of ineffectual treatment
$0.265 (1983 - 1986)	$10.64 - $14.18 Reduced cost of ineffectual treatment
$2.03 (1980 - 1990)	$50.25 - 67.0 Reduces cost of ineffectual treatment

* *Upper value is the best estimate of savings provided by the respective ICDs. Lower value is 75 percent of the best estimate. The adjustment reflects uncertainty with respect to unit costs, adoption rates and the share of changes in incidence or mode of treatment which should be attributed to the NIH-sponsored innovation.*

NIAID formulated haemophilus influenzae type b intervention in 18-month-old infants. The new PRP conjugate vaccine is now 90 percent effective in 18-month-old children. Haemophilus influenzae type b disease is the leading cause of bacterial meningitis in the United States. It also causes a wide spectrum of other serious infections, including bacteremia, epiglottitis, pneumonia, septic arthritis, osteomyelitis, pericarditis and cellulitis. Eighty percent of infants are expected to receive the vaccine. Savings include reduced treatment costs for meningitis and related diseases, reduced lifetime custodial care for the more seriously affected victims, and increased expected lifetime earnings.

NCI developed combination chemotherapy with cisplatin for the treatment of advanced stage testicular cancer. Testicular cancer is the most common malignancy in 15- to 35-year-old males. It is the most frequent cause of cancer-related deaths in this age group. Results of a clinical trial published in 1977 demonstrated that treatment with cisplatin, vinblastine, and bleomycin (PVB) resulted in a complete repsonse rate of 77 percent and a cure rate of 60-65 percent. Those rates were the highest ever reported for this disease. Savings are due to improved survival rates.

NCI made advances in the diagnosis of cutaneous malignant melanoma which have led to earlier detection of melanoma. Early detection results in lower cost treatment, often on an outpatient basis, and in improved survival rates.

Estimated Amount and Duration NIH Applied and Clinical Research Support (millions $)	Estimated Potential 1 Year Savings (millions $ and type of savings)
$15.63 (1972 - 1989)	$109.44 - $145.92 Reduces health care and custodial care/ reduces indirect costs of mortality and morbidity
$55.76 (1970 - 1987)	$109.75 - $146.33 Improved survival/ reduces premature mortality
$17.27 (1971 - 1987)	$87.99 - $117.32 Reduces cost of treatment/ reduces premature mortality

Health Care Cost Savings Resulting from NIH-Supported Research 1989

Health Care Advance

NCI developed an assay which has led to routine screening of the nation's blood supply for HIV antibody. The identification of HIV as the etiologic agent for AIDS made possible the development of a specific assay for the detection of HIV antibodies in the sera of individuals exposed to the virus. In 1983-1984, a specific enzyme immunoassay to detect HIV antibodies was developed in the intramural laboratories of the NCI. Since March 1985, donated blood units have been routinely tested for HIV using this procedure. It is conservatively estimated that the screening annually saves 891 transfusion recipients from HIV infection.

CC proved blood banks can avoid HIV-antigen screening of the nation's donated blood. Clinical Center scientists organized and oversaw a study of almost 500,000 donors nationwide which showed HIV-antigen was *not* detected in HIV-antibody-negative blood. The study helped to avoid the unnecessary adoption of a commercially available kit for screening all 12 million units of blood donated annually in the United States.

CC has improved the diagnostic process for pneumocystis carinii pneumonia (PCP) by use of induced sputum and monoclonal antibodies. The monoclonal antibodies and specimen handling and analysis techniques developed here allow induced sputum specimens to be used to screen for PCP in patients with AIDS and in some cancer patients. The sputum test replaces a more expensive and invasive diagnostic test which requires a bronchoscopy or open lung biopsy.

Estimated Amount and Duration NIH Applied and Clinical Research Support (millions $)	Estimated Potential * 1 Year Savings (millions $ and type of savings)
$6.69 (1984 - 1989)	$47.78 - $63.7 Reduces treatment costs and premature mortality
$0.04 (1988)	$27.0 - $36.0 Avoids cost of unnecessary screening of donated blood
$0.36 (1988 - 1989)	$30.56 - $40.75 Reduces cost ot diagnosis

* *Upper value is the best estimate of savings provided by the respective ICDs. Lower value is 75 percent of the best estimate. The adjustment reflects uncertainty with respect to unit costs, adoption rates and the share of changes in incidence or mode of treatment which should be attributed to the NIH-sponsored innovation.*

NCI developed adjuvant therapy for Dukes' C colon cancer using levamisole and 5-flurouracil. For the more than 22,000 patients annually diagnosed with Dukes' C colon cancer, adjuvant therapy with levamisole and (5-FU) can significantly delay tumor recurrence and reduce the risk of dying of recurrent colon cancer by one-third.

NIAMS combined cytotoxic drug and steroid treatment for lupus nephritis. About 10 percent of the over 10,000 patients diagnosed each year with systemic lupus erythematosus (lupus) develop nephritis and some of those victims eventually develop end-stage renal disease (ESRD). A long-term clinical trial designed and conducted by NIH intramural scientists demonstrated that combined drug regimens that included prednisone with a cytotoxic drug (cyclophosphamide) could sustain life-supporting renal functions beyond 5 years at a significantly greater rate than the use of prednisone alone.

NIDDK advanced successes with renal transplantation. NIH research on transplation and on tissue and organ banking has improved the efficacy and safety of renal transplantation for patients with end-stage renal disease. Annually about 9,100 ESRD patients receive transplants, and this number continues to increase. Compared with maintenance hemodialysis, transplantation improves physical functioning (including ability to remain in the work force), increases life expectancy, and, while the transplanted kidney survives, lowers the average annual treatment costs for the recipient.

Estimated Amount and Duration NIH Applied and Clinical Research Support (millions $)	Estimated Potential * 1 Year Savings (millions $ and type of savings)
$10.84 (1978 - 1990)	$135.98 - $181.31 Reduces loss of work days due to premature mortality
$9.82 (1970 - 1988)	$69.81 - $93.08 Reduces loss of work days and treatment costs
$467.97 (1970 - 1989)	$341.04 - $454.72 Reduces loss of work days and average annual treatment costs

Potential annual health care cost savings in 1989 prices and return ratios resulting from NIH investments in applied research and clinical trials, by health care area and population group (millions of dollars).

Health Care Area	NIH Support *	Annual Savings * *	
		Children	
		low	high
Diagnosis / Screening	28.0	399.8	399.8
New Therapy	681.5	20.5	126.0
Prevention	45.8	126.3	168.4
Evaluation of Existing Practice	20.6	308.0	410.6
Multiple	23.8		
Total	**799.7**	**657.3**	**886.1**
Return Ratio		**17.0**	**22.9**

Summary

Analysis of the examples suggests that the highest savings are found in the areas of diagnosis/screening and evaluation of existing practices. In the former area, $28 million dollars in NIH support as measured in 1989 prices led to savings ranging from **$617.2** to **$689.6**, or a 22 to 24.6 annual return ratio (617.2 divided by 28 and 689.6 divided by 28). The return ratio for the evaluation of existing practices was 20.2 to 27. In terms of population groups, not surprisingly, the health care advances focusing on children had the best return ratio regardless of the type of advancement. The return ratio for children ranged from 17 to 22.9, far outpacing the adult group or the cases involving both groups.

* *1989 prices calculated using BRDPI, 1989 = 100*
** *1989 prices calculated using CPI, 1989 = 100*
*** *Return ratio*

Adults		Combination		Overall	
low	high	low	high	low	high
89.4	119.2	128.0	170.7	617.2	689.6
				22.0***	24.6***
3,864.0	4,697.6	159.1	237.2	4,043.6	5,060.8
				5.9***	7.4***
54.4	108.9	54.5	108.9	180.7	277.3
				3.9***	6.1***
51.2	68.3	57.6	76.8	416.8	555.7
				20.2***	27.0***
210.0	404.3			210.0	404.3
8.8	17.0			8.8***	17.0***
4,157.6	**5,214.0**	**399.1**	**593.6**	**5214.1**	**6693.7**
6.5	**8.2**	**3.2**	**4.8**	**6.5**	**8.4**

The total NIH investment in applied research and clinical trials across all the examples and years amounts to approximately $800 million in 1989 prices. The comparable realizable 1-year savings range from a low of about **$5.2 billion** to a high of nearly **$6.7 billion**. The lower figure suggests an annual rate of potential return of $6.50 for a dollar invested; the higher estimate indicates an $8.40 return for the same dollar.

Technical Appendix

Major features of the cost calculations used in the examples are as follows:

The value of the NIH support costs and savings have been estimated as consistently as possible across the various examples.

For each example, the reported NIH assistance includes one or more clinical trials and frequently several years of applied research. Basic research investments, the benefits of which can not be allocated to a finite group of projects, are excluded as are funds provided from other sources (private firms, nonprofit institutions or other government support) which might have financed part of the clinical trial or applied research.

Savings in most cases are expressed in terms of 1 year's worth of treatment or in terms of the savings to the cohort of new patients for 1 year. Most of these savings will continue from year-to-year as a result of annual incidence rates or of screening and treatment of new births. Multi-year estimates have in most cases not been included because of problems inherent in forecasting.

The reported cost savings are based on the difference between estimated costs before and after the innovation. Prior NIH research investments are not subtracted from the estimated annual savings to arrive at net savings. A stream of such investments over a number of prior years makes up a pool of capital expenditure which yields benefits accruing over several future years. The value of such pooled expenditure is not typically subtracted from 1 year's savings. It is worth noting, however, that estimated 1-year savings for all but one example considerably exceed the associated capitalized value of the NIH support.

Savings are calculated by the human capital approach. This model computes costs in terms of both the direct health care delivery costs and indirect costs expressed as the present discounted value of expected future earnings realized by reduced mortality and morbidity. Valuing lives in this manner is a conservative approach. While placing an economic value on life may be repugnant to some, neglecting to value saved lives or reduced morbidity seriously understates the social benefits of biomedical research.

The cost estimates for the savings examples neglect the indirect costs of time such as lost hours of work, transportation and other expenditures related to morbidity and treatment. In several examples the avoided costs of undesirable side effects are not included in the savings estimates because of uncertain incidence and insufficient data on costs. As a result, the savings estimates are more conservative than they would be if such costs were included.

The listed annual savings reflect experts' judgments regarding the probable rate of adoption of the health care innovation. Such estimates inevitably involve some uncertainty with respect to a number of key parameters, such as unit costs, incidence of illness and treatment, and adoption rates for new technology. Most of the examples include explicit assumption or adjustments for uncertainty with respect to key parameters used to develop estimates. As a further conservative adjustment, a low estimate equal to 75 percent of the final computed annual savings was used in 1988 and 1989.

A copy of any of the complete examples can be obtained by calling Ms. Jean Rayman at 301/496-9285. Further details about any example or about the current and planned investigations of the costs and benefits of NIH-supported biomedical research should be directed to Dr. James Schuttinga at 301/496-5011.